

## Neural substrates of recollection and familiarity in Alzheimer's disease

Sarah Genon§, Eric Salmon\*§, Fabienne Collette§, Christine Bastin§.

\*Centre de la Mémoire, CHU de Liège.

§Centre de Recherches du Cyclotron, Université de Liège, Belgique.

### Introduction

Alzheimer's disease (AD) is characterised by deficits of recollection, with relatively preserved familiarity (e.g., Gallo et al., 2004). fMRI studies in healthy participants suggest that the neural correlates of recollection and familiarity differ, with recollection recruiting additional brain regions in prefrontal, medial temporal, posterior cingulate and inferior parietal cortices by comparison to familiarity (Skinner & Fernandes, 2007). Within the medial temporal lobe, the hippocampus and the posterior parahippocampal gyrus support recollection, whereas familiarity depends on the perirhinal cortex (Eichenbaum, Yonelinas & Ranganath, 2007). However, little is known about the brain regions underlying recollection and familiarity in AD. Therefore, the present study sought to measure directly cerebral activity associated to recollection and familiarity in AD patients and in healthy elderly controls by isolating the processes via the process-dissociation procedure (Jacoby, 1991).

### Methods.

In an event-related fMRI experiment, 17 healthy elderly participants and 25 mild AD patients were administered a recognition memory task according to the process-dissociation procedure. The task includes a condition in which recollection opposes familiarity, allowing to isolate the contribution of the two processes to performance. In an incidental encoding phase, participants saw pairs of unrelated words and were instructed to form a mental image associating the two words to determine which is the largest in size. In the subsequent recognition phase, participants were asked to distinguish between studied pairs (intact) and new pairs that contained either recombined studied words (recombined) or unstudied words (new). In this paradigm, correct 'old' judgments to intact pairs can be given on the basis of recollection (R) and/or familiarity (F) ("inclusion" condition =  $R + F(1 - R)$ ), while incorrect 'old' judgments to recombined pairs is driven by familiarity for the individual words when recollection of the actual studied associations failed ("exclusion" condition =  $F(1 - R)$ ). The recollection contribution to performance was estimated by subtracting the scores in the exclusion condition from the scores in the inclusion condition. Familiarity contribution was then calculated by dividing the scores in the exclusion condition by  $1 - R$ . Brain regions associated to recollection were determined by the contrasting cerebral activity for correct response to intact pairs and brain activity for false alarms to recombined pairs. Brain regions activated during familiarity processes were determined by conjunction of cerebral activity for these two types of events. Preprocessing and statistical analyses were performed with SPM8 ( $p < .05$  corrected for multiple comparisons or  $p < .05$  for small volume correction with a-priori hypotheses).

### Results.

Behavioural results indicated that recollection was impaired in AD patients ( $M = .085$   $SD = .11$ ) compared to healthy controls ( $M = .46$ ,  $SD = .25$ ,  $t(39) = -6.39$ ,  $p < .001$ ). Actually, 12 AD patients have an estimated proportion of recollection equal to zero. Thus, out of 25 AD patients, only 13 patients have engaged residual recollection processes during the associative recognition task. Nevertheless, recollection estimates were poorer in these patients than in the controls ( $M = .13$ ,  $SD = .12$ ,  $t(28) = 4.22$ ,  $p < .001$ ). On the basis of these results, AD patients were divided into two subgroups: a subgroup of patients with residual recollection processes ( $n = 13$ , "AD with recollection") and a subgroup of patients without recollection during the memory task ( $n = 12$ , "AD

patients without recollection”). In contrast, proportion of familiarity was similar in AD ( $M = .57$   $SD = .21$ ) and CTRL group ( $M = .56$   $SD = .20$ ,  $t(39) = .037$   $p = .97$ ), as well as in “AD without recollection” ( $M = .55$   $SD = .21$ ) and in “AD with recollection” group ( $M = .58$   $SD = .22$ ,  $t(22) = -.31$   $p = .76$ ).

fMRI results revealed significant brain activation in parietal, occipital and frontal areas associated with Familiarity in the 3 groups of participants. Recollection was significantly associated with activations of the ventromedial prefrontal cortex (VMPFC, BA10) and the anterior cingulate cortex (ACC, BA24) in AD patients with recollection, but not in controls (at  $p < 0.05$  corrected). SVC analyses performed on brain activation maps for the Recollection contrast revealed significant results for the right posterior hippocampus (HP) in AD patients with recollection ( $p < .01$ ) and in the control group ( $p < .05$ ).

#### Conclusion

In AD patients, recollection was severely impaired but not familiarity. Familiarity processes engaged a neural network including parietal, occipital and frontal areas, as shown in previous fMRI studies in healthy adults (Skinner & Fernandes, 2007). Activations of the VMPFC and ACC were related to recollection process exclusively in AD patients. The VMPFC was specifically associated with recollection process (Skinner & Fernandes, 2007) while the ACC was attributed a role in performance monitoring (MacDonald III et al., 2000). HP activation during recollection indicates retrieval of associative links between information (Slotnick, 2010). Altogether, these results suggest that HP is essential to recollection both in normal aging and AD. However, AD patients did not reach a normal recognition performance, although they recruit additional regions during retrieval. This suggests that, in these patients, HP activity is not sufficient to support totally efficient recollection.

#### References

- Eichenbaum, H., Yonelinas, A.R. & Ranganath, C. (2007), ‘The medial temporal lobe and recognition memory’, *Annual Review of Neurosciences*, vol. 30, pp. 123-152.
- Gallo, D.A., Daffner, K.R., Sullinvan, A.L. & Schacter, D.L. (2004), ‘Associative recognition in Alzheimer’s disease: evidence for impaired recall-to-reject’, *Neuropsychology*, vol. 18, no. 3, 556-563.
- Jacoby, L.L. (1991), ‘A process-dissociation framework: separating automatic from intentional uses of memory’, *Journal of Memory and Language*, vol. 30, no. 5, pp. 513-541.
- MacDonald III, A. W., Cohen, J.D., Stenger, V.A. & Carter, C.S. (2000), ‘Dissociating the Role of the Dorsolateral Prefrontal and Anterior Cingulate Cortex in Cognitive Control’, *Science*, vol. 288, no. 5472, pp. 1835-1838.
- Skinner, E.I. & Fernandes, M.A. (2007), ‘Neural correlates of recollection and familiarity: a review of neuroimaging and patient data’, *Neuropsychologia*, vol. 45, no. 10, pp. 2163-2179.
- Slotnick, S.D. (2010), ‘Does the hippocampus mediate objective binding or subjective remembering?’, *NeuroImage*, vol. 49, no. 2, pp. 1769-1776.